



DEVELOPMENT AND *IN-VITRO* EVALUATION STUDIES OF NIOSOMAL GEL FORMULATIONS

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Govind^{1*}, Atul Sharma², Dr. Sachin Kumar³

¹Research scholar, Department of Pharmaceutics, N.K.B.R College of Pharmacy & Research Centre, Meerut, Uttar Pradesh -245206, India.

²Assistant Professor, Department of Pharmaceutics, N.K.B.R College of Pharmacy & Research Centre, Meerut, Uttar Pradesh -245206, India.

³Professor, Department of Pharmaceutics, N.K.B.R College of Pharmacy & Research Centre, Meerut, Uttar Pradesh -245206, India.

*Corresponding Author : Govind, Department of Pharmaceutics, N.K.B.R College of Pharmacy & Research Centre, Meerut, Uttar Pradesh -245206, India. Email Id: govindpal8516@gmail.com

ABSTRACT

Psoriasis is a widespread skin disease affecting 2-3 per cent of the world 's population. It can be identified as a condition of inflammatory skin marked by an abnormal proliferation and differentiation. Niosome preparation using Film Hydration method drug 100 mg and Surfactant: Cholesterol Ratio (0.5: 0.5-1.5) Total 9 Batches were prepared. The drug was pre-evaluated for its compatibility studies for HPMC, SPAN, Carbapol, sodium alginate, guar gum and xanthan gum. Span 20 gave drug content 83.1±1.1 to 91.8±2.6 mg; Span 60 gave 90.3±1.6 to 93.9±1.5mg and Span 80 gave 93.1±1.5 to 85.1±1.0 mg. All the assessment was done in replicate. NF5 formulation corresponds to the higher drug content and entrapment efficiency. The NF5 formulation carried forward for the preparation of gel formulations, total 10 formulations F1-F10 were prepared and subjected to evaluation. Among all the formulations the gel formed F5 and F6 were found to be clearest with better spreadability and with excellent homogeneity. F6 were found to be highest viscosity among all the other formulation batches i.e. 8166 cPs. Batch F-6 was found as optimized formulation, which is further subjected to stability studies and pharmacological studies. For the evaluation of in vivo anti psoriatic studies the animals were divided into 4 groups Group I: Negative Control (No Disease), Group II: Positive Control (Diseased but receive no, treatment, Group III: Receive Blank Gel as treatment, Group IV: Receive Best formulation as treatment. Niosomal gel of Tacrolimus showed lowest PASI score among the treatment group. Along with the when it is compared with that of negative group. From the study it is evident that niosomal gel of Tacrolimus formulation containing carbapol 934, 4 mg showed a promising results for the treatment of psoriasis.

Keywords: Niosomal, Tacrolimus , Carbapol, Psoriasis.

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I. INTRODUCTION

Psoriasis can appear at any time, and it has been recorded at birth and in elderly people. About 2 per cent of the population is affected in the U.S. High psoriasis levels were recorded in the Faroe Islands, in which survey reported 2.8 percent of the total population infected Niosome is a non-ionic

surfactant-based vesicle which is formed mostly by non-ionic surfactant and cholesterol incorporation as an excipient. First reported the niosomes as a feature of the cosmetic industry, The characteristics of the vesicle formulation are variable and controllable. Altering vesicle composition, size, lamellarity, tapped volume, surface charge and concentration can control the vesicle



characteristics.¹⁻⁵ The association of amphiphile monomers into vesicles on hydration is the result of high interfacial tension between water and hydrocarbon portion (or any other hydrophobic group) of the amphiphile, causing them to associate. Carbopol polymers are high molecular weight, cross linked, acrylic acid based polymer.⁶⁻¹² Sodium alginate (NaC₆H₇O₆) is a linear polysaccharide derivative of alginic acid comprised of 1,4-β-d-mannuronic (M) and α-l-guluronic (G) acids.

II. MATERIALS AND METHODS

Melting Point:

The melting points of the drugs were determined by an open capillary method using the melting point apparatus.

Partition Coefficient (K_p):

The partition coefficient of the drug was determined by shaking equal volumes of oil and the aqueous phase in a separating funnel. A drug solution of 1 mg/ml was prepared in distilled water, and 50 ml of this solution was taken¹²⁻¹⁶ in a separating funnel and shaken with an equal volume of octanol for 10 min and allowed to stand for 24 h with intermittent shaking. Then, the aqueous phase was assayed before and after partitioning using a UV spectrophotometer to get the partition coefficient values .

Preliminary solubility studies of drug

10 mg of (API) was weighed and solubility was checked in 10 ml water, methanol, 0.1 N NaOH and 0.1 N HCl. The drug was found to be freely soluble in inorganic solvents as sulphuric acid, hydrochloric acid, acetonitrile etc. but practically poorly soluble in water, 0.1 N NaOH. Therefore, HCl and water (60:40 % v/v) was selected as diluent as they are freely available and drug was also found to be stable in methanol for 24 hours in stability studies.

Scanning Electron Microscopy (SEM) study

The optimized niosomal formulation was characterized for their morphology using

scanning electron microscope.¹⁷⁻¹⁹ The lyophilized samples of niosomes was sprinkled and fixed in a SEM holder with double sided adhesive tape and coated by a layer of gold of 150^oA for 5 to 6 minutes using sputter coater, under a vacuum voltage.

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Preparation of stock solution

Standard stock solution of pure drug containing 1000 µg/ml of tacrolimus prepared in HCl and distilled water in 60:40% v/v. The working standard solutions of the drug were obtained by dilution of the stock solution in the distilled water. Series of solutions with conc. 2, 4, 6, 8, 10, 12, 14, 16, 18 and 20 µg/ml of Tacrolimus were used to prepare calibration curve. Solutions were scanned and proposed methods were applied for the determination of area under curve. Methanol and Water 60:40 % v/v was used as blank solution.

Preparation of sample stock solution:

Drug equivalent to 100 mg was transferred into a 100 ml volumetric flask (1000 µg/ml). From this 10 ml was withdrawn and diluted upto 100 ml with solvent. From this further 1 ml was diluted up to 10 ml and used as stock solution¹⁵⁻²⁰.

III. RESULTS AND DISCUSSION

The Icalibration graph for Tacrolimus was generated using Tacrolimus 2-20 µg/ mL solution in DMSO. They measured the absorbance at 291 nm. Figure 4.2 showed the calibration Igraph for Tacrolimus. Table 1 showed the absorbance achieved for the given concentrations. A regression equation $Y = 0.01726 * X + 0.02473$ and R² value 0.9977 is shown in the calibration curve (Table 1). The result found that the concentration of drugs around 2-20 µg / ml followed the law of Beer Lambert, as the coefficients of regression was 0.9977 was shown in Fig. 1.



Table 1: FTIR findings of pure Tacrolimus drug.

Band Frequency	Functional Groups
3883.08	OH Streching
3583.04	OH Streching
3031.71	OH Streching
2925.78	NH Streching
1737.35	CH Stretching Alkene
1543.69	O=C=O Stretching
1450.91	C-H Bending
1282.81	N-O Stretching
1237.62	C(O)-O stretching vibrations and -OH in plane vibrations/amide III
1187.48	C-O stretching
1080.26	C-H bending

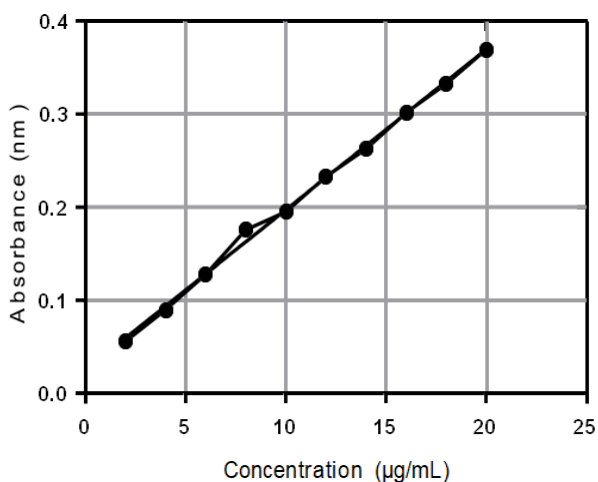


Fig. 1: Coefficients of regression was

0.9977 of Tacrolimus drug.

Pure obtained drug tacrolimus was subjected to FTIR analysis. The graph generated between wavelength and transmission percentage was observed and interpretation of peak observed were performed. As per the interpretation results sharp peaks were observed at 3883.08, 3583.04, 3031.71, 2925.78, 1737.35, 1543.69, 1450.91, 1282.81, 1237.62, 1187.48, 1080.26, 921.75, 805.18. These peaks were observed corresponds to the various bond energies of difference functional groups. These functional groups were found in accordance with the structure of Tacrolimus pure was shown in Fig 2. This is sample was then examined with a scanning electron microscope (Quanta Feg) at 10KV accelerate voltage.

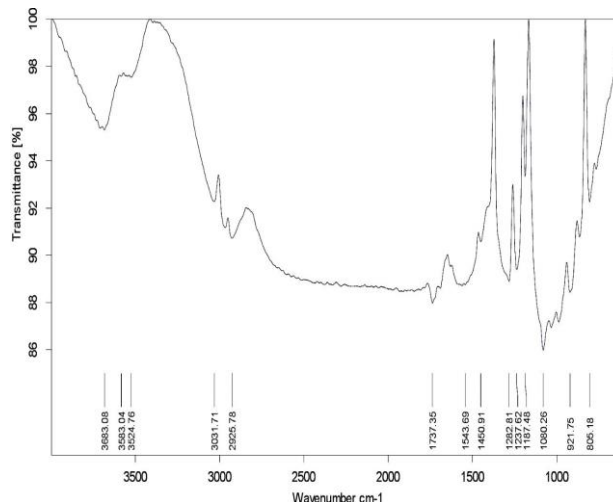


Fig. 2: FTIR Spectra of Tacrolimus drug sample.

Three polymer i.e. Span, Carbapol and HPMC were used for the preparation of Niosomes and gel respectively. Drug Tacrolimus was subjected to undergo the compatibility study with the polymers with the help of IR Spectrophotometry. Drug Tacrolimus was mixed with polymer and IR Spectrum were observed for the presence of additional peaks other than pure Tacrolimus and Polymer alone was shown in Figure 4.



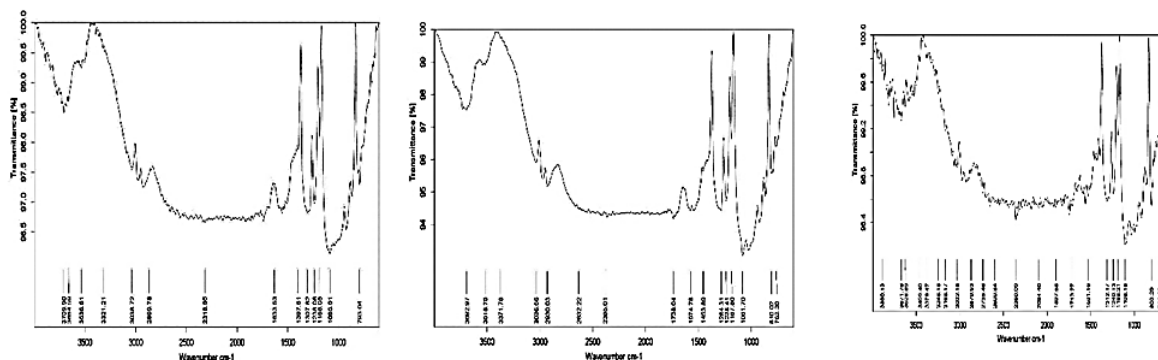


Fig. 4: R Spectrum of Tacrolimus & Carbopol IR Spectrum of Tacrolimus and HPMC IR Spectrum of Tacrolimus and Span.

All the planned clumps of Tacrolimus Niosomal Gel were exposed to skin disturbance test on dermal tissue. Applications were made for 7 successive days. For every creature, dermal reaction scores at 1 h, 24 h, 48 and 72 h after evacuation of the test materials. added and

afterward separated by three to acquire a mean aggravation score for every time point. The outcomes were contrasted with those of the control creatures which got refined water. The mean scores were added and arrived at the midpoint of to acquire the essential disturbance file was shown in Table 2.

Table 2: DSC comparative data of Tacrolimus excipients.

DSC	Onset (°C)	Peak (°C)	Endset (°C)
Pure drug	123.03	130.11	138.55
Tac.+ span	122.27	130.16	137.73
Tac.+ carbopol	121.64	130.36	138.94
Tac.+ HPMC	122.40	131.42	138.16

Stability Studies:

The optimized Niosomal Gel formulation F6 was subjected to stability studies over the period of 6 months. The formulation was evaluated for Drug content, pH and % drug release over the period. The formulation was attributed to have 93.9

±1.5 mg drug content at the starting 0 month, which found to be 93.8 ± 1.8 at the 6th month. There is no significant difference between the drug content in mean time interval was shown in Table 3.

Table 3: Stability Studies of Optimized Niosome Gel formulation.

Parameters	Months				
	0	1	2	3	6
Drug content (mg)	93.9 ± 1.5	94.1 ± 0.50	93.7 ± 1.2	94.01± 0.43	93.8 ± 1.8
pH	6.2	6.1	6.2	6.1	6.3
(%) Drug release	64 ± 1.24	66.17± 0.23	65.24± 1.24	65.8 ± 1.8	63.17 ± 1.9
Physical appearance	Transparent Consistent Gel				



IV. CONCLUSION

Characterization of the drug through FTIR showed corresponding peaks structural elements of Tacrolimus, which also confirmed the tacrolimus. DSC thermogram of pure drug was obtained which showed an endothermic peak at 130.11°C. Tacrolimus mixture with polymers like Carbopol, HPMC and SPAN were subjected to the analysis by FTIR and DSC for their interaction with drug. The results showed that there was no interaction found between the two. Niosomes of the drug tacrolimus were prepared using various surfactant: cholesterol ratio and total 9 batches of niosomes were prepared. And as per the results of particle size, drug content and entrapment efficiency the NF-5 batch was found most suitable and further used for the preparation of gel batches. Total 10 batches of the niosomal gel were formulated and characterized. As per the characterization parameters batch F-6 was found as optimized formulation, which is further subjected to stability studies and pharmacological studies. The stability studies showed a non-changing parameters over the course of study of 6 months. Also the blank gel formulation was subjected to evaluation in Group III which showed no significant changes in the score before and after the course of treatment. This evident the good penetration of drug through the corresponding formulation and apart from the API the other formulating agent remains inactive for their pharmacodynamic properties. Also from the in-vitro release study it was evident that optimized formulation of Tacrolimus gel, demonstrated a controlled release profile $I(92.46 \pm 2.16)$ over the 48 h period. Controlled release profile of Tacrolimus niosome gel may be due to slow diffusion of Tacrolimus in the Carbopol matrix from lipid niosome. This evident the proposed composition using API Tacrolimus can be used as novel topical formulation for the treatment of Psoriasis.

Conflict of Interest

Not applicable

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